JACC Vol. 5, No. 6
June 1985:190B-191B

Clinical Problems Relevant to Sudden Death: Discussion

Moderator: **Robert O. Brandenburg, MD, FACC;** *Panelists:* **Valentin Fuster, MD, FACC, Bernard J. Gersh, MD, FACC, Lawrence E. Hinkle, Jr., MD, FACC, Frits L. Meijler, MD, FACC, Michael F. Oliver, MD, FACC, T. Joseph Reeves, MD, FACC, Lino Rossi, MD, Jack L. Titus, MD, PhD**

Dr. Brandenburg: Dr. Fuster, in your discussion on the development of the atherosclerotic lesion, fat is not mentioned until the fifth stage. Does this fact have something to do with the rather disappointing effects of fat reduction in the diet for controlling the problem of atherosclerosis?

Dr. Fuster: There are five biological ways in which fat plays important roles in the atherosclerotic process.

1. A high serum concentration of low density lipoprotein appears to contribute to the process of endothelial injury.
2. Some studies with smooth muscle cell cultures suggest that lipoproteins may be mitogenic, contributing to cell membrane formation.
3. The space occupying fat accumulations may contribute to the growth of the atherosclerotic plaque.
4. Factors impairing removal of cholesterol from the arterial wall appear to favor its accumulation and, hence, progression of the disease.
5. Evidence has been presented indicating lipoproteins may enhance platelet reactivity explaining the increased thrombogenicity of an ulcerated plaque.

In addition to the biological process, there are the epidemiologic aspects in a disease like atherosclerosis.

Dr. Brandenburg: Dr. Reeves, what is your approach to the patient with mild stable angina pectoris whose echocardiogram discloses normal left ventricular function? Are additional studies indicated?

Dr. Reeves: I would like to see the results of a stress test. Also, exercise echocardiography is being developed.

Dr. Oliver: With respect to the role of lipids in atherosclerosis, studies of twins indicate that 55 to 59% of the cholesterol level is genetically determined. In view of this, we must take into account the other aspects of the genetic transmission of lipoprotein abnormalities. Perhaps the endothelial receptor systems have been underemphasized.

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Dr. Meijler: Dr. Fuster, why do many people who do not develop unstable angina, myocardial infarction or sudden death seem to lead the same type of life as those who do?

Dr. Fuster: Most investigators consider atherosclerotic disease a biological reaction of the artery to chronic injury. Early lesions are seen at autopsy in almost everyone older than the age of 40 to 50 years. However, only selected people develop clinically important lesions. Young patients who have clinically significant coronary artery disease almost invariably have a strong family history of first degree relatives with coronary artery disease and have a very high incidence of being cigarette smokers. These factors appear to accelerate the disease process. However, it is certainly true that individuals aged 60 to 65 years who have a myocardial infarction may have no risk factors.

Dr. Rossi: With respect to the classification of cardiomyopathies, I would mention so-called right ventricular dysplasia. I believe that since this is an acquired disease of unknown cause, we could call it RVD, but interpret the "D" as disease, rather than dysplasia.

Dr. Hinkle: In the Coronary Artery Surgery Study (CASS), prognosis was related first to the functional state of the left ventricle, but beyond that it was related to the number of vessels occluded, the degree of occlusion and the location of the occlusion. Angina pectoris, whether present or absent, was not an independent indicator of risk. In view of this, Dr. Reeves, what would the indication be for performing coronary angiography if there was no angina pectoris and no evidence of impaired left ventricular function?

Dr. Reeves: I draw attention to the study of Kent and Epstein in patients with triple vessel disease who were asymptomatic or only mildly symptomatic and had normal ventricular function. In the high risk group with a shortened exercise stress test, the annual mortality rate could be as high as 9%.

Dr. Hinkle: I was referring to a population group of individuals and trying to determine how to identify people with significant coronary artery disease. I gather this would

0735-1097/85/$3.30

be done primarily by noting abnormalities in the rest electrocardiogram or obtaining a stress test.

Dr. Reeves: In addition, I would identify major risk factors such as a strong family history of coronary disease, cigarette smoking and hypertension.

Dr. Titus: Minimal thickening of the arterial wall should not be termed atherosclerosis. This term is appropriate only when there has been progression beyond the thickening. (Dr. Fuster agreed.)

Dr. Gersh: I am pleased to hear Dr. Fuster make a strong argument in support of sudden death in many instances masking the underlying or precipitating event. Perhaps in determining the therapeutic strategy for sudden death, one of the major considerations would be that active ischemia, either overt or covert, is present.

Question from the audience: How would you rationalize therapy for patients who have postinfarction angina, particularly in regard to anticoagulation?

Dr. Fuster: In the effort to prevent myocardial infarction, platelet inhibitor therapy would seem appropriate where there are rapid changes in the atherosclerotic lesion and in patients with unstable angina. In patients with unstable angina, three studies—a European study of heparin, a U.S. study of aspirin and a Canadian study of aspirin—disclosed the same result. There was a 50 to 60% reduction in the incidence of myocardial infarction or sudden death within 12 weeks. This is the group of patients that I believe should receive antithrombotic therapy. The duration of this therapy is not yet clear. I do not advise the use of platelet inhibitor drugs in patients with chronic coronary artery disease.